REMARKS

Claims 1, 3-19 and 21-24 currently are pending. Claims 1, 6, 7, 18, and 21 have been amended. Claims 2 and 20 have been canceled. Claims 22-24 have been newly added.

**35 USC § 112, second paragraph**

The examiner stated claim 1 is indefinite. Applicant respond by amending claim 1 to recite "excipients" instead of "other conventional excipients."

Applicants delete "preferably ..." from claim 6 and add a new claim (22) directed to the deleted subject matter.

Claims 7 and 8 were rejected because they recite a narrow recitation which falls within a broad recitation in the same claim. Applicants delete the narrower limitations and add dependent claims to the deleted subject matter.

Applicants delete claim 20 and amend claim 21 into a proper statutory claim.

Claims 1, 4-7 and 9-21 are rejected under 35 USC § 102(b) as being anticipated by Grabowski et al. (5,490,990). Anticipation can only be established by a single prior art reference which discloses each and every element of the claimed invention. *RCA Corp. v. Applied Digital Systems Inc.,* 730 F.2d 1440, 1444, 221 USPQ 385, 388) (Fed. Cir. 1984). Grabowski et al. disclose a formulated mixture comprising a copolymer, for example polyvinylacetate and a spraying aid for example polyvinylpyrrolidone **or** cellulose derivatives. The present claims how require the **combination** of all three components. In the inventive dosage form, a water soluble such as hydroxypropylmethylcellulose is added

to a formulated mixture of polyvinylpyrrolidone and polyvinylacetate after spray drying of the mixture. The combination of the three components simplifies compression.

Claims 1-21 are rejected under 35 USC § 102(b) as being anticipated by Kolter et al. (US 6,066,634). Kolter et al. disclose a **rapid** release pharmaceutically active composition wherein the formulated mixture comprises polyvinyl acetate, N-vinylpyrrolidone, a water soluble and a water insoluble polymer. The present pharmaceutical composition, however, shows a **delayed** release of the active ingredient which results from the use of a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone. This formulated mixture wherein the PVP acts as a protective colloid for the polyvinyl acetate has different molecular interactions and is more suitable for release slowing than mixtures wherein the water-soluble polymer is added separately into the tablet. Also, the content is restricted from 0.5 to 20%, whereas the content of the formulated mixture according to the invention is preferably from 20 to 60% and the ratio of polyvinyl acetate and polyvinylpyrrolidone in the formulated mixture is between 6:4 and 9:1. Applicants amend claim 1 by incorporating the subject matter of claim 2.

The examiner rejected claims 1-5, 8-12 and 15-21 under 35 USC § 102(b) as being anticipated by Ortega (4,837,032). Ortega et al. disclose a theophylline tablet comprising polyvinylpyrrolidone and polyvinyl acetate but there is no formulated mixture of PVP and polyvinyl acetate disclosed. This results in less mechanical stability in the tablets. Therefore, Ortega et al. do not disclose each and every element of the present invention.

Claims 1, 4-7, and 9-21 were rejected under 35 USC § 103(a) as being unpatentable over Grabowski et al. (5,490,990). because the examiner believes the manipulation of amounts of ingredients would have been obvious to one skilled in the art at the time of the invention with the motivation of adjusting amounts in accordance with requirements to maintain anti-blocking properties of the composition while adjusting other contents of the formulation such as amount of drugs or additives.

One of the basic requirements of a *prima facie* case of obviousness is that the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143. As stated above, in the inventive oral dosage form a water soluble polymer, such as hydroxypropylmethylcellulose is added in addition to a formulated mixture of polyvinylpyrrolidone and polyvinylacetate after spraying drying of the mixture. The **combination** of the **three** components simplifies compression. This is neither taught nor suggested by Grabowski et al. To achieve the advantageous properties of the inventive combinations it is of great importance that the three components, if they are pressed into a tablet, are still in the form of individual particles. Only then can the special features such as high mechanical stability can occur, because of the molecular interaction.

Claims 1-21 are rejected under 35 USC § 103(a) as being unpatentable over Kolter et al. As stated above, Kolter et al. disclose a **rapid** release pharmaceutically active composition wherein the formulated mixture. The inventive pharmaceutical composition shows a delayed release of the active ingredient which results from the use of a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone. This formulated mixture wherein the

PVP acts as a protective colloid for the polyvinyl acetate has different molecular interactions and is more suitable for release slowing than mixtures wherein the water-soluble polymer is added separately into the tablet. The difference is supported by the hardness of the tablets. The hardness in Kolter et la. is 93 N and 48 N and the tablets thus have a lower mechanical stability. Since Kolter et al. neither teach nor suggest this feature of the present invention there is no obviousness of the present claims.

Claims 1-5, 8-12 and 15-21 are rejected under 35 USC § 103(a) as being unpatentable over Ortega (US 4,837,032). Although Ortega et al. disclose a theophylline tablet comprising polyvinylpyrrolidone and polyvinyl acetate, there is no formulated mixture of polyvinylpyrrolidone and polyvinyl acetate that results in the hardness achieved by the present invention. The hardness of the tablets in Ortega et al. is 40-100 N. The hardness of the inventive tablets is over 200N and the friability is small than 0.1%. Therefore, applicants believe the present claims are not rendered obvious by Ortega et al.

Claims 1-21 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-16 of US 6,066,034. Applicants disagree with the examiner's view that rapid release is a subjective term and the reference also requires that release occurs up to an hour later. Kolter et al. disclose a rapid release pharmaceutically active composition wherein the formulated mixture comprises polyvinyl acetate, N-vinylpyrrolidone, a water soluble and a water insoluble polymer. The present pharmaceutical composition, however, shows a **delayed** release of the active ingredient which results from the use of a formulated mixture of polyvinyl acetate and

polyvinylpyrrolidone. This formulated mixture wherein the PVP acts as a protective colloid for the polyvinyl acetate has different molecular interactions and is more suitable for release slowing than mixtures wherein the water-soluble polymer is added separately into the tablet. Also, the content is restricted from 0.5 to 20%, whereas the content of the formulated mixture according to the invention is preferably from 20 to 60% and the ratio of polyvinyl acetate and polyvinylpyrrolidone in the formulated mixture is between 6:4 and 9:1.

For the reasons expressed above, it is urged that the prior art references cited by the examiner either singly or in combination fail to anticipate or suggest the present invention as defined by the amended claims. Accordingly, a *prima facie* case of obviousness has not been established by the examiner, and the rejection under 35 USC § 103 should be withdrawn.

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Respectfully submitted,
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***VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE CLAIMS***

Please amend claims 1,6,7,18, 21 and newly added claims 22 -24 as follows:

1. (amended) An oral dosage form with delayed release of active ingredient and high mechanical stability, comprising

a) one or more active ingredients

b) a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone

c) water-soluble polymers or low or high molecular weight lipophilic additives

d) and other conventional excipients,

wherein the ratio of polyvinyl acetate to polyvinylpyrrolidone is from 6:4 to 9:1.

6. (amended) An oral dosage form as claimed in claim 1, wherein the water-soluble or lipophilic polymers are selected from the group consisting of: polyvinyl alcohols, polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones and derivatives, and vinyl acetate/vinylpyrrolidone copolymers[, preferably polyethylene glycols, polyvinylpyrrolidones, vinyl acetate/vinylpyrrolidone copolymers or maltodextrins, and salts thereof].

7. (amended) An oral dosage form as claimed in claim 1, wherein the water-soluble swelling polymers are selected from the group consisting of: alginates, pectins, galactomannans, carrageenans, dextran, curdlan, pullulan, gellan, chitin, gelatin, xanthans, hemicelluloses, cellulose derivatives [such as methylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, methylhydroxyethylcellulose, carboxymethylcellulose,] and starch [derivatives such

as carboxymethyl starch, degraded starch, polyacrylic acid, polymethacrylic acid, acrylic acid/methacrylic acid copolymers,] and salts thereof.

8. (amended) An oral dosage form as claimed in claim 1, wherein the lipophilic additives are selected from the group consisting of: cellulose derivatives [such as ethylcellulose, cellulose acetate, cellulose acetate phthalate, cellulose acetate succinate, hydroxy propylmethylcellulose acetate phthalate, hydroxypropylmethylcellulose acetate succinate], acrylic ester/methacrylic ester copolymers, [in particular methyl methacrylate/ethyl acrylate copolymers, ammoniomethacrylate copolymer type A and type B, methacrylic acid/acrylic ester copolymers, in particular methacrylic acid/ethyl acrylate copolymers,] fatty alcohols [such as stearyl alcohol], fatty acids [such as stearic acid], fatty acid esters and fatty alcohol esters, glycerides, waxes, and lecithin.

18. [A] The dosage form as claimed in claim 1, wherein the active pharmaceutical ingredient is selected from the group consisting of benzodiazepines, antihypertensives, vitamins, cytostatics, anesthetics, neuroleptics, antidepressants, antibiotics, antimycotics, fungicides, chemotherapeutics, urologicals, platelet aggregation inhibitors, sulfonamides, spasmolytics, hormones, immunoglobulins, sera, thyroid therapeutics, psychopharmaceuticals, antiparkinson agents and other antihyperkinetics, ophthalmologicals, neuropathy products, calcium metabolism regulators, muscle relaxants, lipid-lowering agents, liver therapeutics, coronary agents, cardiac agents, immunotherapeutics, regulatory peptides and their

inhibitors, hypnotics, sedatives, gynecologicals, antigout agents, fibrinolytics, enzyme products and transport proteins, enzyme inhibitors, emetics, perfusion promoters, diuretics, diagnostics, corticoids, cholinergics, biliary therapeutics, antiasthmatics, bronchospasmolytics, beta-receptor blockers, calcium channel blockers, ACE inhibitors, arteriosclerosis remedies, antiinflammatory agents, anticoagulants, antihypotensives, antihypoglycemics, antifibrinolytics, antiepileptics, antiemetics, antidotes, antidiabetics, antiarrhythmics, antianemics, antiallergics, anthelmintics, analgesics, analeptics, aldosterone antagonists, and weight-reducing agents.

21. [The use of t] Food supplements or additives, or vitamins, minerals or trace elements comprising the oral dosage form[s] as claimed in claim 1 for delayed release of active ingredients [which are food supplements or additive, vitamins, minerals or trace elements].

22. (newly added) An oral dosage form as claimed in claim 6 wherein the water-soluble or lipophilic polymers are selected from the group consisting of polyethylene glycols, polyvinylpyrrolidones, vinyl acetate/vinylpyrrolidone copolymers or maltodextrins, and salts thereof.

23. (newly added) The oral dosage form as claimed in claim 7, wherein the cellulose derivatives are selected from the group consisting of methylcellulose, methylhydroxyethylcellulose, carboxymethylcellulose and wherein the starch derivatives are selected from the group consisting of carboxymethyl starch,

degraded starch, polyacrylic acid, polymethacrylic acid, acrylic acid/methacrylic acid copolymers.

24. (newly added) The oral dosage form as claimed in claim 8, wherein the lipophilic additives are selected from the group consisting of cellulose derivatives which are ethylcellulose, cellulose acetate, cellulose acetate phthalate, cellulose acetate succinate, hydroxy propylmethylcellulose acetate phthalate, or hydroxypropylmethylcellulose acetate succinate, acrylic ester/ethacrylic ester copolymers which are methyl methacrylate/ethyl acrylate copolymers, ammoniomethacrylate copolymer type A and type B, methacrylic acid/acrylic ester copolymers or methacrylic acid/ethyl acrylate copolymers, fatty alcohols which are stearyl alcohols, fatty acids which are stearic acid, fatty acid esters and fatty alcohol esters, glycerides, waxes and lecithin.